10/081400

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PTO/SB/21 (07-06)
Approved for use through 09/30/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	Patent#: 7,101,971
Filing Date	Issued: September 5, 2006
First Named Inventor	Harry M. Meade
Art Unit	1632
Examiner Name	J. T. Woitach
Total Number of Pages in This Submission	
Attorney Docket Number	G0744.70030US02

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Certificate of Correction

Remarks

Request for Certificate of Correction,
Certificate of Correction,
Pages of USPN 7,101,971 marked in red, and
Return Receipt Postcard

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	Janice A. Vatland		
Printed name	Janice A. Vatland		
Date	January 19, 2007	Reg. No.	52,318

Certificate of Mailing Under 37 CFR 1.8(a)

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Dated: 1-19-07 Signature: _____ (Michelle M. Quinn)

Docket No.: G0744.70030US02
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Harry M. Meade et al.
Serial No.:	10/081,400
Confirmation No.:	3033
Filed:	February 20, 2002
Patent No.:	7,101,971
For:	ERYTHROPOIETIN ANALOG-HUMAN SERUM ALBUMIN FUSION
Examiner:	J. T. Woitach
Art Unit:	1632

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Dated: 1-19-07

Michelle M. Quinn

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.322

Attention: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted typographical errors which should be corrected.

In the Claims:

In Claim 1, line 41, delete "glycosylation glycosylation" and insert -- glycosylation --

In Claim 2, line 44, delete "EPOa.hSA" and insert --EPOa-hSA--

In Claim 2, line 46, delete "orR1-L-R2 L-R1" and insert --or R1-L-R2-L-R1--

In Claim 2, line 47, delete "og" and insert --analog--

In Claim 2, line 48, delete “h” and insert --human--

In Claim 3, line 51, delete “pep de” and insert --peptide--

In Claim 4, line 53, delete “sequenc” and insert --sequence--

In Claim 5, line 56, delete “EPOa.hSA” and insert --EPOa-hSA--

In Claim 7, line 62, delete “2 or” and insert --2 or 3--

In Claim 8, line 66, delete “ent” and insert --attachment--

In Claim 10, line 39, delete “EPOa-hS” and insert --EPOa-hSA--

In Claim 10, line 40, delete “up” and insert --group--

In Claim 11, line 43, delete “Serl2” and insert --Ser126--

In Claim 12, line 45, delete “BPOa-hSA" and insert --EPOa-hSA--

In Claim 12, line 46, delete “saud” and insert --said--

In Claim 12, line 48, delete “Am” and insert --Asn--

In Claim 13, line 51, delete “Gin.” and insert --Gln.--

In Claim 15, line 57, delete “Gin” and insert --Gln--

In Claim 15, line 58, delete “has replaced” and insert --has been replaced--

In Claim 16, line 60, delete “fusion protein” and insert --the fusion protein--

In Claim 16, line 61, delete “GlnS3” and insert --Gln83--

In Claim 16, line 62, delete “hwnan” and insert --human--

In Claim 17, line 64, delete "GIn24,iGIn3S, GIn83," and insert --Gln24, Gln38, Gln83,--

In Claim 17, line 65, delete "apeptide" and insert --a peptide--

In Claim 17, line 66, delete "Gly-Gly-$(Gly)_3$-Ser-Pro)" and insert --Gly-Gly-Gly)$_3$-Ser-Pro)--

In Claim 17, line 67, delete "albwnin" and insert --albumin--

In Claim 18, line 2, delete "teft to" and insert --left to--

In Claim 19, line 7, delete "EPOs" and insert --EPOa--

In Claim 20, line 3, delete "peptido" and insert --peptide--

In Claim 20, line 3, delete " ((Ser-Gly.Gly-Gly-Gly)$_3$- " and insert -- ((Ser-Gly-Gly-Gly-Gly)$_3$- --

In Claim 20, line 4, delete "Ala 126" and insert --Ala126--

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Patentee respectfully solicits the granting of the requested Certificate of Correction. Applicant believes no fee is required.

Dated: January 19, 2007

Respectfully submitted,

By _____
Janice A. Vatland
Registration No.: 52,318
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
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Boston, Massachusetts 02210-2206
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PTO/SB/44 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,101,971

APPLICATION NO. : 10/081,400

ISSUE DATE : September 5, 2006

INVENTOR(S) : Harry M. Meade et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Claim 1, line 41, delete "glycosylation glycosylation" and insert -- glycosylation --

In Claim 2, line 44, delete "EPOa.hSA" and insert --EPOa-hSA--

In Claim 2, line 46, delete "orR1-L-R2 L-R1" and insert --or R1-L-R2-L-R1--

In Claim 2, line 47, delete "og" and insert --analog--

In Claim 2, line 48, delete "h" and insert --human--

In Claim 3, line 51, delete "pep de" and insert --peptide--

In Claim 4, line 53, delete "sequenc" and insert --sequence--

In Claim 5, line 56, delete "EPOa.hSA" and insert --EPOa-hSA--

In Claim 7, line 62, delete "2 or" and insert --2 or 3--

In Claim 8, line 66, delete "ent" and insert --attachment--

In Claim 10, line 39, delete "EPOa-hS" and insert --EPOa-hSA--

In Claim 10, line 40, delete "up" and insert --group--

In Claim 11, line 43, delete "Serl2" and insert --Ser126--

In Claim 12, line 45, delete "BPOa-hSA" and insert --EPOa-hSA--

In Claim 12, line 46, delete "saud" and insert --said--

In Claim 12, line 48, delete "Am" and insert --Asn--

In Claim 13, line 51, delete "Gin." and insert --Gln.--

In Claim 15, line 57, delete "Gin" and insert --Gln--

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JAN 24 2007

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(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

In Claim 15, line 58, delete "has replaced" and insert --has been replaced--

In Claim 16, line 60, delete "fusion protein" and insert --the fusion protein--

In Claim 16, line 61, delete "GlnS3" and insert --Gln83--

In Claim 16, line 62, delete "hwnan" and insert --human--

In Claim 17, line 64, delete "GIn24,iGIn3S, GIn83," and insert --Gln24, Gln38, Gln83,--

In Claim 17, line 65, delete "apeptide" and insert --a peptide--

In Claim 17, line 66, delete "Gly-Gly-$(Gly)_3$-Ser-Pro)" and insert --Gly-Gly-Gly)$_3$-Ser-Pro)--

In Claim 17, line 67, delete "albwnin" and insert --albumin--

In Claim 18, line 2, delete "teft to" and insert --left to--

In Claim 19, line 7, delete "EPOs" and insert --EPOa--

In Claim 20, line 3, delete "peptido" and insert --peptide--

In Claim 20, line 3, delete " ((Ser-Gly.Gly-Gly-Gly)$_3$- " and insert -- ((Ser-Gly-Gly-Gly-Gly)$_3$- --

In Claim 20, line 4, delete "Ala 126" and insert --Ala126--

Certificate of Mailing Under 37 CFR 1.8(a)

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Dated: _____ Signature: _____ (Michelle M. Quinn)

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Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206

JAN 24 2007

-continued

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Gly Gly Gly Gly
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<210> SEQ ID NO 4
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1 5 10 15

Pro

What is claimed is:

1. An EPOa-hSA fusion protein, wherein the EPOa moiety is the full coding region of the human EPO sequence but wherein each amino acid residue of the EPOa moiety that serves as a site for glycosylation of the fusion protein is altered such that such a site does not serve as a site for glycosylation ~~glycosylation~~ in the EPOa; and,

wherein both the albumin moiety and the EPOa moiety of the fusion protein is derived from a human sequence.

2. The ~~EPOa-hSA~~ fusion protein of claim 1, wherein said fusion protein has the formula:

R1-L-R2; R2-L-R1; orR1-L-R2-L-R1, wherein R1 is an erythropoietin ~~og~~ amino acid sequence; L is a peptide linker and R2 is a ~~h~~ serum albumin amino acid sequence.

3. The EPOa-hSA fusion protein of claim 2, wherein R1 and R2 are covalently linked via said ~~pep-de~~ linker.

4. The EPOa-hSA fusion protein of claim 3, wherein said peptide linker is composed of a sequence having the formula (Ser-Ser-Ser-Ser-Gly)y (SEQ. ID 5) wherein y is less than or equal to 8.

5. The ~~EPOa-hSA~~ fusion protein of claim 3, wherein said peptide linker is 10 to 30 amino acids in length.

6. The EPOa-hSA fusion protein of claim 5, wherein each of said amino acids in said peptide linker is selected from the group consisting of Gly, Ser, Asn, Thr and Ala.

7. The EPOa-hSA fusion protein of claim 5, wherein said peptide linker is composed of either 2 or 3 tandem repeats of a sequence having the formula $((Ser\text{-}Ser\text{-}Ser\text{-}Ser\text{-}Gly)_3\text{-}Ser\text{-}Pro$ (SEQ. ID 4).

8. The EPOa-hSA fusion protein of claim 1, wherein each amino acid residue which serves as an ~~ept~~ point for glycosylation has been deleted.

9. The EPOa-hSA fusion protein of claim 1, wherein each amino acid residue of human EPO which serves as a site for glycosylation has been replaced with an amino acid residue which does not serve as a site for glycosylation.

10. The EPOa-hSA fusion protein of claim 1, wherein said amino acid residue is selected from the ~~up~~ consisting of amino acid residues Asn24, Asn38, Asn83 and Ser126.

11. The EPOa-hSA fusion protein of claim 1, wherein said glycosylation sites altered include ~~Ser12~~ Asn24, Asn38 and Asn83.

12. The ~~EPOa-hSA~~ fusion protein of claim 1, wherein ~~said~~ glycosylation sites altered are either O-linked or N-linked glycosylation sites and are altered by replacing an amino acid residue ~~Asn~~ or Ser with a Gln residue.

13. The EPOa-hSA fusion protein of claim 1, wherein each of the amino acid residues 24, 38, 83 and 126 have been replaced with ~~Gln~~.

14. The EPOa-hSA fusion protein of claim 1, wherein each of the amino acid residues 24, 38, 83 and 126 have been deleted.

15. The EPOa-hSA fusion protein of claim 14, wherein each of the amino acid residues 24, 38 and 83 have been replaced with ~~Gln~~ and wherein said amino acid residue 126 has replaced with Ala.

16. The EPOa-hSA fusion protein of claim 1, wherein fusion protein includes from left to right, an EPOa which includes amino acid residues Gln24, Gln38, ~~Gln83~~ and Ala126, a peptide linker, and ~~hwnan~~ serum albumin.

17. The EPOa-hSA fusion protein of claim 1, wherein the fusion protein is from left to right, ~~Gln24,iGln38, Gln83,~~ Ala126 EPO, ~~apeptide~~ linker having the formula ((Ser-Gly-Gly-Gly-~~(Gly)3 Ser-Pro~~) (SEQ. ID 4) and human serum ~~albwnin~~ albumin.

JAN 24 2007

procedure is identical to that outlined for embryo collection outlined above, except that the oviduct is not cannulated, and the embryos are transferred in a minimal volume of Ham's F12 containing 10% FBS into the oviductal lumen via the fimbria using a glass micropipet. Animals having more than six to eight ovulation points on the ovary are deemed unsuitable as recipients. Incision closure and post-operative care are the same as for donor animals (see, e.g., Selgrath, et al., Theriogenology, 1990. pp. 1195–1205).

Monitoring of pregnancy and parturition

Pregnancy is determined by ultrasonography 45 days after the first day of standing estrus. At Day 110 a second ultrasound exam is conducted to confirm pregnancy and assess fetal stress. At Day 130 the pregnant recipient doe is vaccinated with tetanus toxoid and Clostridium C&D. Selenium and vitamin E (Bo-Se) are given IM and Ivermectin was given SC. The does are moved to a clean stall on Day 145 and allowed to acclimatize to this environment prior to inducing labor on about Day 147. Parturition is induced at Day 147 with 40 mg of PGF2a (Lutalyse®, Upjohn Company, Kalamazoo Michigan). This injection is given IM in two doses, one 20 mg dose followed by a 20 mg dose four hours later. The doe is under periodic observation during the day and evening following the first injection of Lutalyse® on Day 147. Observations are increased to every 30 minutes beginning on the morning of the second day. Parturition occurred between 30 and 40 hours after the first injection. Following delivery the doe is milked to collect the colostrum and passage of the placenta is confirmed.

Verification of the transgenic nature of F_0 animals:

To screen for transgenic F_0 animals, genomic DNA is isolated from two different cell lines to avoid missing any mosaic transgenics. A mosaic animal is defined as any goat that does not have at least one copy of the transgene in every cell. Therefore, an ear tissue sample (mesodem) and blood sample are taken from a two day old F_0 animal for the isolation of genomic DNA (Lacy, et al., A Laboratory Manual, 1986, Cold Springs Harbor, N.Y.; and Hermmann and Frischauf, Methods Enzymology, 1987. 152: pp. 180–183). The DNA samples are analyzed by the polymerase chain reaction (Gould, et al., Proc. Natl. Acad. Sci, 1989. 86:pp. 1934–1938) using primers specific for human EPOa-hSA fusion protein gene and by Southern blot analysis (Thomas, Proc Natl. Acad. Sci., 1980. 77:5201-5205) using a random primed EPO or hSA cDNA probe (Feinberg and Vogelstein, *Anal. Bioc.*, 1983. 132: pp. 6–13). Assay sensitivity is estimated to be the detection of one copy of the transgene in 10% of the somatic cells.

Generation and Selection of production herd

The procedures described above can be used for production of transgenic founder (F_0) goats, as well as other transgenic goats. The transgenic F_0 founder goats, for example, are bred to produce milk, if female, or to produce a transgenic female offspring if it is a male founder. This transgenic founder male, can be bred to non-transgenic females, to produce transgenic female offspring.

Transmission of transgene and pertinent characteristics

Transmission of the transgene of interest, in the goat line is analyzed in ear tissue and blood by PCR and Southern blot analysis. For example, Southern blot analysis of the founder male and the three transgenic offspring shows no rearrangement or change in the copy number between generations. The Southern blots are probed with human EPOa-hSA fusion protein cDNA probe. The blots are analyzed on a Betascope 603 and copy number determined by comparison of the transgene to the goat beta casein endogenous gene.

Evaluation of expression levels

The expression level of the transgenic protein, in the milk of transgenic animals, is determined using enzymatic assays or Western blots.

Other embodiments are within the following claims.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 4

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated linker sequence; subsets 2 through 8 (each consisting of a repetition of the first five amino acids) encompassing positions 6 through 40 may be absent or present

<400> SEQUENCE: 1

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Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
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Gly Gly Gly Ser Gly Gly Gly Gly
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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetically generated linker sequence

18. The EPOa-hSA fusion protein of claim **1**, wherein the EPOa-hSA fusion protein includes, from ~~left to~~ right, human serum albumin, a peptide linker, and an EPOa which includes amino acid residues Gln24, Gln38, Gln83 and Ala126.

19. The EPOa-hSA fusion protein of claim **18**, wherein the ~~EPOa~~ is Gln24, Gln38, Gln83, Ala126 EPO.

20. The EPOa-hSA fusion protein of claim **1**, wherein the fusion protein is from left to right, human serum albumin, a ~~peptide~~ linker having the formula (~~(Ser-Gly-Gly-Gly-Gly)$_3$~~-Ser-Pro) (SEQ. ID 4), and Gln24, Gln38, Gln83, ~~Ala126~~ EPO.

* * * * *